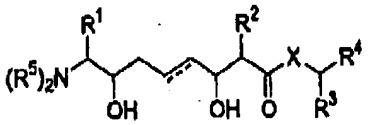
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior listings of claims in the application.

1. (currently amended) A compound of the formula (I):



(I)

wherein,

each R^1, R^2, and R^3 are independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

X is N~~, O, or S~~;

R^4 is H, $CON(R^7)_2$, $CONHR^7$, CH_2OH, $CH(OH)CH{=}CH_2$, or $C(O)NHCHR^{10}CO_2H$;

each R^5 is independently H, alkyl, alkenyl, aryl, heteroaryl, acyl, P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^2;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{10} is independently an amino acid side chain;

each P^1 and P^2 is independently a nitrogen protecting group; and

each P^3 is independently an oxygen protecting group;

or pharmaceutically acceptable salts thereof.

2. (currently amended) The compound of claim 1, wherein:

X is N ~~or O~~;

R^1 is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

R^4 is H, $CON(R^7)_2$, $C(O)NHCHR^{10}CO_2H$, or CH_2OH;

each R^5 is independently H, alkyl, acyl, P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^2;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{10} is independently an amino acid side chain;

each P^1 and P^2 is independently a nitrogen protecting group; and

each P^3 is independently an oxygen protecting group.

3. (currently amended) The compound of claim 1, wherein:

X is N ~~or O~~;

R^1 is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, halo, or C_{1-6} alkyl;

R^4 is H, $CONHR^7$, or CH_2OH;

each R^5 is independently H or alkyl;

each R^6 is independently H or alkyl;

R^7 is H, alkyl, or P^2; and

P^2 is a nitrogen protecting group.

4. (currently amended) The compound of claim 1, wherein:

X is N ~~or O~~;

R^1 is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OH or C_{1-6} alkyl; and

R_4 is H, $CONH_2$, or CH_2OH.

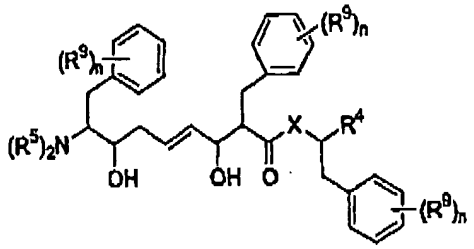
5. (currently amended) The compound of claim 1, wherein:

X is N ~~or O~~;

R^1 is C_1 alkyl substituted with phenyl, which is substituted at the 2- and 6- positions with Me and is substituted at the 4- position with OH; and

R^4 is H, $CONH_2$, or CH_2OH.

6. (currently amended) The compound of claim 1 having the formula (II):



(II)

wherein,

X is N ~~or O~~;

R^4 is H, $CON(R^7)_2$, $CONHR^7$, CH_2OH, or $C(O)NHCHR^{10}CO_2H$;

each R^5 is independently H, alkyl, acyl, P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^2;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^9 is independently OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

each R^{10} is independently an amino acid side chain;

each n is independently 0, 1, 2, 3, 4, or 5;

each P^1 and P^2 is independently a nitrogen protecting group; and

each P^3 is independently an oxygen protecting group.

7. (original) The compound of claim 6, wherein:

R^4 is H, $CON(R^7)_2$, $CONHR^7$, or CH_2OH;

each R^5 is independently H, alkyl, or acyl;

each R^6 is independently H or alkyl;

each R^7 is independently H or alkyl;

each R^9 is independently OR^6, CN, NO_2, halo, or C_{1-6} alkyl; and

each n is independently 0 1, 2, or 3.

8. (original) The compound of claim 6, wherein:

P^1 is a BOC or Fmoc;

P^2 is a solid support; and

P^3 is *t*-Bu, Bn, Me, or Ac.

9. (original) The compound of claim 6, wherein:

R^4 is H, $CON(R^7)_2$, $CONHR^7$, or CH_2OH;

each R^5 is independently H, alkyl, acyl, or P^1;

each R^6 is independently H or P^3;

each R^7 is independently H or P^2;

each R^9 is independently OR^6 or C_{1-6} alkyl;

each n is independently 0, 1, or 2;

P^1 is a BOC;

P^2 is a solid support; and

P^3 is *t*-Bu.

10. (original) The compound of claim 6, wherein:

R^4 is H, $CONH_2$, or CH_2OH;

each R^5 is independently H, P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is H or alkyl

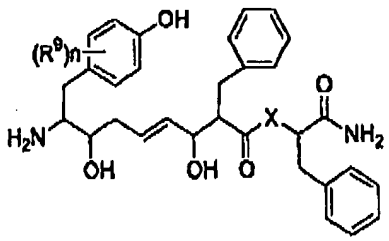
each R^9 is C_{1-6} alkyl or OR^6;

each R^{10} is independently an amino acid side chain;

each n is independently 1, 2, or 3; and

P^1 is a nitrogen protecting group.

11. (currently amended) The compound of claim 1 that is formula (III):



(III)

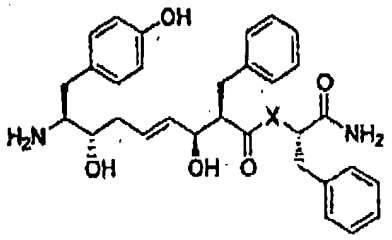
wherein,

X is ~~O or~~ N;

R^9 is C_{1-6} alkyl; and

n is 2.

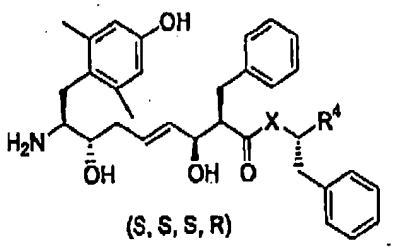
12. (currently amended) The compound of claim 1 that is formula (IV):



(IV)

wherein X is N ~~or O~~.

13. (currently amended) The compound of claim 1 having the formula (V):



(S, S, S, R)

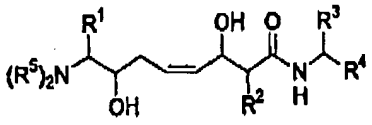
(V)

wherein

X is N ~~or O~~; and

R^4 is $CONH_2$, H, or CH_2OH.

14. (original) The compound of claim 1 having the formula (VI):



(VI)

wherein,

each R^1, R^2, and R^3 is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

R^4 is H, $CON(R^7)_2$, $CONHR^7$, CH_2OH, or $CH(OH)CH{=}CH_2$, or $C(O)NHCHR^{10}CO_2H$;

each R^5 is independently H, alkyl, alkene, aryl, heteroaryl, acyl, or P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^2;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{10} is independently an amino acid side chain;

each P^1 and P^2 is independently a nitrogen protecting group; and

each P^3 is independently an oxygen protecting group.

15. (original) The compound of claim 14, wherein:

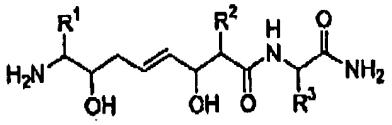
each R^1, R^2, and R^3 is independently alkyl substituted with aryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, halo, or C_{1-6} alkyl;

R^4 is H, $CON(R^7)_2$, or $CONHR^7$, or $C(O)NHCHR^{10}CO_2H$;

each R^5 is independently H, alkyl, acyl, P^1, or $C(O)CHR^{10}NH_2$; and

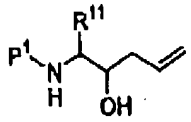
each R^{10} is independently an amino acid side chain.

16. (original) A method of making a compound of the formula (VIII):

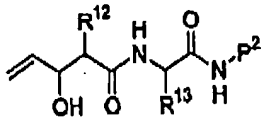


(VIII)

comprising coupling compounds of the formulas (XI) and (XII)

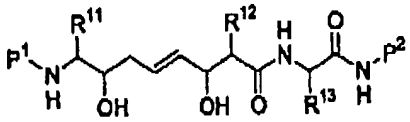


(XI)



(XII)

using a ruthenium catalyst, to give a compound of formula (IX); and



(IX)

reacting the compound of formula (IX) with a deprotecting agent to give a compound of the formula (VIII);

wherein,

each R^1, R^2, and R^3 is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^4;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{11}, R^{12}, and R^{13} is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^{16}, CN, NO_2, NHR^{17}, $N(R^{17})_2$, halo, $CONHR^{17}$, $CON(R^{17})_2$, CO_2R^{18}, or C_{1-6} alkyl;

each R^{16} is independently H, alkyl, or P^3;

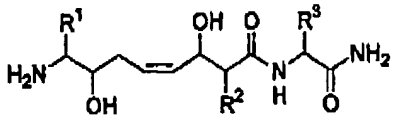
each R^{17} is independently H, alkyl, acyl, or P^4;

each R^{18} is independently H, alkyl, aralkyl, or heteroaralkyl;

each P^1, P^2, and P^4 is independently a nitrogen protecting group; and

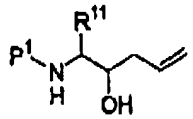
each P^3 is independently an oxygen protecting group.

17. (original) A method of making a compound of the formula (XVI):

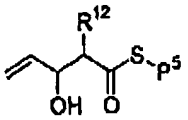


(XVI)

comprising coupling compounds of the formulas (XI) and (XIII)

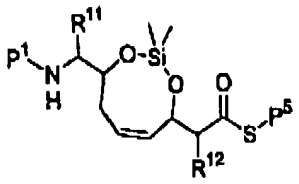


(XI)



(XIII)

by first reacting the free alcohols with a silicon protecting group, and then treating the resulting compound with a ruthenium catalyst, giving a compound of the formula (VII);



(VII)

reacting the compound of formula (VII) under pH conditions sufficient to remove acid labile protecting groups, if any;

treating the resulting product with peroxide and base under conditions sufficient to hydrolyze the thioester; and

coupling the resulting product with a solid phase peptide, giving a compound of the formula (XVI);

wherein,

each R^1, R^2, and R^3 is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^4;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{11} and R^{12} is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^{16}, CN, NO_2, NHR^{17}, $N(R^{17})_2$, halo, $CONHR^{17}$, $CON(R^{17})_2$ CO_2R^{18}, or C_{1-6} alkyl;

each R^{16} is independently H, alkyl, or P^3;

each R^{17} is independently H, alkyl, acyl, or P^4;

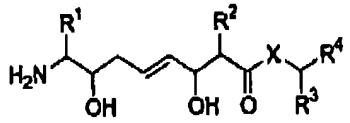
each R^{18} is independently H, alkyl, aralkyl, or heteroaralkyl;

each P^1 and P^4 is independently a nitrogen protecting group; and

each P^3 is independently an oxygen protecting group; and

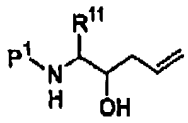
P^5 is a sulfur protecting group.

18. (currently amended) A method of making a compound of the formula (XIV):

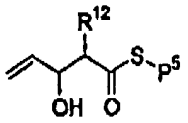


(XIV)

comprising coupling compounds of formulas (XI) and (XIII),



(XI)



(XIII)

with a ruthenium catalyst;

treating the resulting compound with peroxide and base under conditions sufficient to hydrolyze the thioester;

amidation or esterification of the resulting acid; and

treatment of the resulting compound with a deprotecting agent sufficient to remove protecting groups, giving a compound of the formula (XIV);

wherein,

each R^1, R^2, and R^3 is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

X is N ~~or O~~;

R^4 is H, $CON(R^7)_2$, $CONHR^7$, CH_2OH, or $CH(OH)CH{=}CH_2$;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^4;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{11} and R^{12} are independently alkyl substituted with aryl or heteroaryl, each of

which is optionally substituted with 1-5 substituents selected from OR^{16}, CN, NO_2, NHR^{17}, $N(R^{17})_2$, halo, $CONHR^{17}$, $CON(R^{17})_2$, CO_2R^{18}, or C_{1-6} alkyl;

each R^{16} is independently H, alkyl, or P^3;

each R^{17} is independently H, alkyl, acyl, or P^4;

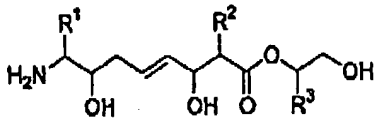
each R^{18} is independently H, alkyl, aralkyl, or heteroaralkyl;

each P^1 and P^4 is independently a nitrogen protecting group;

each P^3 is independently an oxygen protecting group; and

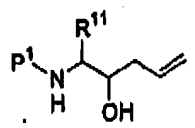
P^5 is a sulfur protecting group.

19. (original) A method of making a compound of formula (XVII):

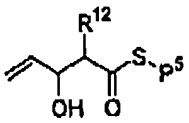


(XVII)

comprising coupling compounds of formulas (XI) and (XIII)



(XI)

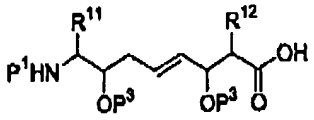


(XIII)

with a ruthenium catalyst;

treating the resulting compound with peroxide and base under conditions sufficient to hydrolyze the thioester; and

reacting the free hydroxyls with an oxygen protecting group to give a compound of formula (XVIII)



(XVIII)

coupling the compound of formula (XVIII) with an alcohol of formula $R^{13}(CHOH)CHOR^{16}$; and

treating the resulting compound with a deprotecting agent sufficient to remove protecting groups to give a compound of formula (XVII);

wherein,

each R^1, R^2, and R^3 is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^4;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{11}, R^{12}, and R^{13} is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^{16}, CN, NO_2, NHR^{17}, $N(R^{17})_2$, halo, $CONHR^{17}$, $CON(R^{17})_2$ CO_2R^{18}, or C_{1-6} alkyl;

each R^{16} is independently H, alkyl, or P^3;

each R^{17} is independently H, alkyl, acyl, or P^4;

each R^{18} is independently H, alkyl, aralkyl, or heteroaralkyl;

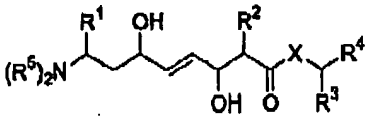
each P^1 and P^4 is independently a nitrogen protecting group;

each P^3 is independently an oxygen protecting group; and

P^5 is a sulfur protecting group.

20. (original) A composition comprising a compound of formula (I) in claim 1 and a pharmaceutically acceptable carrier.

21. (currently amended) A compound of formula (XIX):



(XIX)

wherein,

each R^1, R^2, and R^3 is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$ halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

X is N~~, O, or S~~;

R^4 is H, $CON(R^7)_2$, $CONHR^7$, CH_2OH, $CH(OH)CH=CH_2$, or $C(O)NHCHR^{10}CO_2H$;

each R^5 is independently H, alkyl, alkenyl, aryl, heteroaryl, acyl, P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^2;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{10} is independently an amino acid side chain;

each P^1 and P^2 is independently a nitrogen protecting group;

each P^3 is independently an oxygen protecting group; and

or pharmaceutically acceptable salts thereof.

22. (currently amended) The compound of claim 21 wherein:

X is N or ~~O~~;

R^1 is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

R^4 is H, $CON(R^7)_2$, $C(O)NHCHR^{10}CO_2H$, or CH_2OH; and

each R^5 is independently H, alkyl, acyl, P^1, or $C(O)CHR^{10}NH_2$;

each R^{10} is independently an amino acid side chain.

23. (currently amended) The compound of claim 21, wherein:

X is N ~~or O~~;

R^1 is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, halo, or C_{1-6} alkyl;

R^4 is H, $CONHR^7$, or CH_2OH;

each R^5 is independently H or alkyl;

each R^6 is independently H or alkyl; and

R^7 is H, alkyl, or P^2.

24. (currently amended) The compound of claim 21, wherein:

X is N ~~or O~~;

R^1 is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OH or C_{1-6} alkyl; and

R^4 is H, $CONH_2$, or CH_2OH.

25. (currently amended) The compound of claim 21, wherein:

X is N ~~or O~~;

R^1 is C_1 alkyl substituted with phenyl, which is substituted at the 2- and 6- positions with Me and is substituted at the 4- position with OH; and

R^4 is H, $CONH_2$, or CH_2OH.

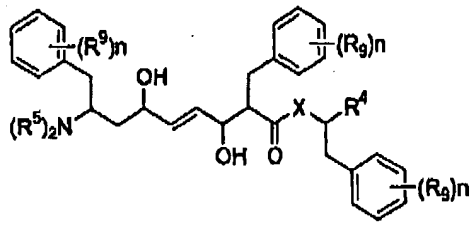
26. (original) The compound of claim 21, wherein

X is N;

R^1 is methyl substituted with phenyl, which is substituted at the 4- position with OH; and

R^4 is $CONH_2$.

27. (currently amended) The compound of claim 21 having the formula (XX):



(XX)

wherein,

X is N ~~or O~~;

R^4 is H, $CON(R^7)_2$, $CONHR^7$, CH_2OH, or $C(O)NHCHR^{10}CO_2H$;

each R^5 is independently H, alkyl, acyl, P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl; or P^2;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^9 is independently OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

each R^{10} is independently an amino acid side chain;

each n is independently 0, 1, 2, 3, 4, or 5;

each P^1 and P^2 is independently a nitrogen protecting group; and

each P^3 is independently an oxygen protecting group.

28. (original) The compound of claim 27, wherein:

R^4 is H, $CON(R^7)_2$, $CONHR^7$, or CH_2OH;

each R^5 is independently H, alkyl, or acyl;

each R^6 is independently H or alkyl;

each R^7 is independently H or alkyl;

each R^9 is independently OR^6, CN, NO_2, halo, or C_{1-6} alkyl; and

each n is independently 0 1, 2, or 3.

29. (original) The compound of claim 27, wherein:

R^4 is H, $CON(R^7)_2$, $CONHR^7$, or CH_2OH;

each R^5 is independently H, alkyl, acyl, or P^1;

each R^6 is independently H or P^3;

each R^7 is independently H or P^2;

each R^9 is independently OR^6 or C_{1-6} alkyl;

each n is independently 0 or 1;

P^1 is a BOC;

P^2 is a solid support; and

P^3 is *t*-Bu.

30. (original) The compound of claim 27, wherein:

R^4 is H, $CONH_2$, or CH_2OH;

each R^5 is independently H, P^1, or $C(O)CHR^{10}NH_2$;

each R^6 is H or alkyl

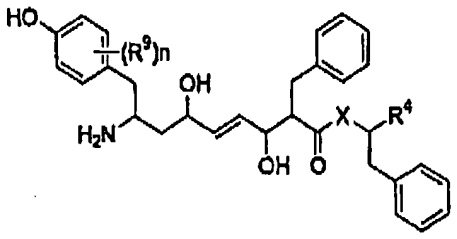
each R^9 is C_{1-6} alkyl or OR^6;

each R^{10} is independently an amino acid side chain;

each n is independently 1, 2, or 3; and

P^1 is a nitrogen protecting group.

31. (currently amended) The compound of claim 21 having the formula (XXI):



(XXI)

wherein,

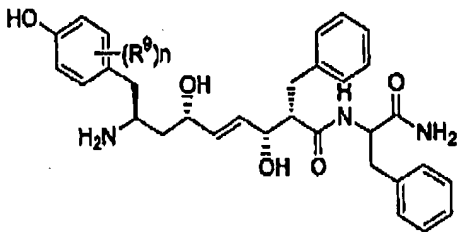
X is ~~O or~~ N;

R^4 is H, $CONH_2$, or CH_2OH;

R^9 is C_{1-6} alkyl; and

n is 2.

32. (original) The compound of claim 21 having the formula (XXII):



(S, S, R, S)

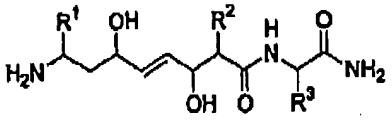
(XXII)

wherein

R^2 is C_{1-6} alkyl; and

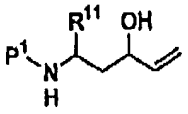
n is 0, 1, or 2.

33. (original) A method of making a compound of formula (XXIII):

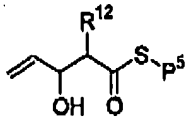


(XXIII)

comprising coupling compounds of formulas (XXV) and (XIII)



(XXV)



(XIII)

using a ruthenium catalyst, giving a compound of the formula (XXIV);

treating the resulting product with peroxide and base under conditions sufficient to hydrolyze the thioester;

coupling the resulting product with a solid phase peptide; and

treating the resulting compound with a deprotecting agent, giving a compound of the formula (XXIII);

wherein,

each R^1, R^2, and R^3 is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^6, CN, NO_2, NHR^7, $N(R^7)_2$, halo, $CONHR^7$, $CON(R^7)_2$, CO_2R^8, or C_{1-6} alkyl;

each R^6 is independently H, alkyl, or P^3;

each R^7 is independently H, alkyl, acyl, or P^4;

each R^8 is independently H, alkyl, aralkyl, or heteroaralkyl;

each R^{11} and R^{12} is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR^{16}, CN, NO_2, NHR^{17}, $N(R^{17})_2$, halo, $CONHR^{17}$, $CON(R^{17})_2$, CO_2R^{18}, or C_{1-6} alkyl;

each R^{16} is independently H, alkyl, or P^3;

each R^{17} is independently H, alkyl, acyl, or P^4;

each R^{18} is independently H, alkyl, aralkyl, or heteroaralkyl;

each P^1 and P^4 is independently a nitrogen protecting group;

each P^3 is independently an oxygen protecting group; and

P^5 is a sulfur protecting group.

34. (original) A composition comprising a compound of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier.

35. (currently amended) A method of treating a mu opioid receptor (MOR) mediated disorder that is pain in a subject comprising administering a compound of formula (I) in claim 1 or a compound of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof.

36. (currently amended) A method of treating a mu opioid receptor (MOR) mediated disorder that is pain in a subject comprising administering a composition comprising a compound of formula (I) in claim 1 or a compound of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof.

37. (original) A method of treating pain in a subject, comprising administering to the subject a compound of formula (I) in claim 1 or of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof.

38. (cancelled)